

Search CTL/CD8+ T-Cell Epitope Database

| | | |
|-----------------|--|---|
| HIV Protein | Proteins with defined epitopes - ALL - p17 p17-p24 p24 p24-p2p7p1p6 | Proteins with undefined epitopes - ALL - Gag Gag/Pol Pol Vif |
| Epitope | VLYQYMDDV | |
| Subtype | - ALL - | |
| Immunogen | - ALL - computer prediction HIV-1 and GBV-C co-infection HIV-1 and HCV co-infection HIV-1 exposed seronegative HIV-1 infected monocyte-derived HIV-1 infection | |
| Vaccine details | If Immunogen is Vaccine, additional search details Vaccine type: - ALL - Vaccine strain: - ALL - Vaccine component: - ALL - Adjuvant: - ALL - | |
| Species | - ALL - | |
| MHC/HLA | - ALL - A*01 A*0101 A*02 A*02.01 A*0201 A*020101 | |
| Author | <input type="checkbox"/> First <input type="checkbox"/> Last | |
| Country | - ALL - | |
| Keywords | - ALL - acute/early infection adjuvant comparison antagonism antibody generation assay standardization/improvement binding affinity | |

Search

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Search CTL/CD8+ T-Cell Epitope Database

| | | |
|-----------------|--|--|
| HIV Protein | <div>Proteins with defined epitopes</div> <div> - ALL - p17 p17-p24 p24 p24-p2p7p1p6 </div> | <div>Proteins with undefined epitopes</div> <div> - ALL - Gag Gag/Pol Pol Vif </div> |
| Epitope | VIYOYMDLI | |
| Subtype | - ALL - | |
| Immunogen | - ALL - computer prediction HIV-1 and GBV-C co-infection HIV-1 and HCV co-infection HIV-1 exposed seronegative HIV-1 infected monocyte-derived HIV-1 infection | |
| Vaccine details | <div>If Immunogen is Vaccine, additional search details</div> <div> Vaccine type: - ALL - Vaccine strain: - ALL - Vaccine component: - ALL - Adjuvant: - ALL - </div> | |
| Species | - ALL - | |
| MHC/HLA | - ALL - A*01 A*0101 A*02 A*0201 A*0201 A*020101 | |
| Author | <input type="checkbox"/> First <input type="checkbox"/> Last | |
| Country | - ALL - | |
| Keywords | - ALL - acute/early infection adjuvant comparison antagonism antibody generation assay standardization/improvement binding affinity | |

Search CTL/CD8+ T-Cell Epitope Database

Found 33 matching records:

Displaying record number 466

| | | |
|-----------------------------|----------------------------|--------------------------|
| <u>HXB2 Location</u> | RT(175-199) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | RT(342-366 LAI) | |
| <u>Epitope</u> | NPDIVIIYQYMDDLYVGSDLEIGQHR | <u>Epitope Alignment</u> |
| <u>Subtype</u> | B | |
| <u>Species (MHC/HLA)</u> | human(A11) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Experimental methods</u> | | |
| <u>Keywords</u> | | |

Notes

- One of five epitopes defined for RT-specific CTL clones in this study.

References

Menendez-Arias1998 L. Menendez-Arias, A. Mas, and E. Domingo. Cytotoxic T-lymphocyte responses to HIV-1 reverse transcriptase (review). *Viral Immunol.*, 11:167-81, 1998. PubMed ID: [10189185](#). [Show all entries for this paper.](#)

Walker1989 B. D. Walker, C. Flexner, K. Birch-Limberger, L. Fisher, T. J. Paradis, A. Aldovini, R. Young, B. Moss, and R. T. Schooley. Long-term culture and fine specificity of human cytotoxic T-lymphocyte clones reactive with human immunodeficiency virus type 1. *Proc. Natl. Acad. Sci. U.S.A.*, 86:9514-9518, 1989. Seven HIV-1 reverse transcriptase-specific cytotoxic T-lymphocyte (CTL) clones from the peripheral blood of two seropositive subjects were generated. Five different HLA restricted CTL epitopes were identified by peptide mapping. PubMed ID: [2480604](#). [Show all entries for this paper.](#)

Displaying record number 54572

| | | |
|-----------------------------|---|--------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | RT(179-187) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Epitope Name</u> | VL9 | |
| <u>Subtype</u> | B | |
| <u>Species (MHC/HLA)</u> | human(A*02) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Country</u> | United States | |
| <u>Experimental methods</u> | Intracellular cytokine staining, Other | |
| <u>Keywords</u> | rate of progression, escape, immune evasion | |

Notes

- To correlate evolving HIV-1 populations with HLA-A2 restricted immune responses for epitopes in Gag, Pol, Env and Nef, 11 treatment-naive subjects were longitudinally studied. Results show that increased viral load is often associated with broad CTL responses early in infection that persist as an "immunological footprint". Conversely, early, restricted responses may help limit viral load. Phylogenetic and functional evidence of viral escape is seen in Gag, Nef and Pol. Gag and Nef show flanking epitope changes restricted by non-HLA-A2 alleles. As far as modes of viral adaptation, CTL responses were seen to develop both against static viral populations resulting in viral evolution to HLA-A2 as well as against existing mutants resulting in reselection of consensus B-like variants. This study reinforces that CTL immune responses detected are not necessarily beneficial to patients, but may be "footprints" from early effective responses that the virus has since escaped.

References

Karlsson2007 Annika C. Karlsson, Astrid K. N. Iversen, Joan M. Chapman, Tulio de Oliveira, Gerald Spotts, Andrew J. McMichael, Miles P. Davenport, Frederick M. Hecht, and Douglas F. Nixon. Sequential Broadening of CTL Responses in Early HIV-1 Infection Is Associated with Viral Escape. *PLoS ONE*, 2:e225, 2007. PubMed ID: [17311088](#). [Show all entries for this paper.](#)

Displaying record number 468

| | | |
|-----------------------------|---------------|--------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | RT | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Species (MHC/HLA)</u> | human(A*0201) | |
| <u>Immunogen</u> | vaccine | |
| <u>Experimental methods</u> | | |
| <u>Keywords</u> | | |

Vaccine Details

Vaccine type vaccinia

Notes

- This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans.

References

Hanke1998b T. Hanke, T. J. Blanchard, J. Schneider, G. S. Ogg, R. Tan, M. Becker, S. C. Gilbert, A. V. Hill, G. L. Smith, and A. McMichael. Immunogenicities of intravenous and intramuscular administrations of modified vaccinia virus Ankara-based multi-CTL epitope vaccine for human immunodeficiency virus type 1 in mice. *J. Gen. Virol.*, 79:83-90, 1998. PubMed ID: [9460927](#). [Show all entries for this paper.](#)

Hanke1998c T. Hanke, J. Schneider, S. G. Gilbert, A. V. S. Hill, and A. McMichael. DNA multi-CTL epitope vaccines for HIV and Plasmodium falciparum: Immunogenicity in mice. *Vaccine*, 16:426-435, 1998. PubMed ID: [9607066](#). [Show all entries for this paper.](#)

Displaying record number 470

| | | |
|-----------------------------|-----------------|--------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | RT | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Species (MHC/HLA)</u> | human(A*0201) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Experimental methods</u> | | |
| <u>Keywords</u> | | |

Notes

- Adoptive transfer of two autologous *in vitro*-expanded CTL clones against the A*0201 restricted epitopes SLYNTVATL and VIYQYMDDL were infused into a patient -- they were well tolerated, but the SLYNTVATL clone was shown by tetramer staining to be rapidly eliminated through apoptosis, and the treatment had no impact upon viral load and CD4 and CD8 cell counts.
- Tetramer staining failed for the VIYQYMDDL epitope as the tetramer was unstable.

References

Tan1999 R. Tan, X. Xu, G. S. Ogg, P. Hansasuta, T. Dong, T. Rostron, G. Luzzi, C. P. Conlon, G. R. Screaton, A. J. McMichael, and S. Rowland-Jones. Rapid death of adoptively transferred T cells in acquired immunodeficiency syndrome. *Blood*, 93:1506-10, 1999. PubMed ID: [10029578](#). [Show all entries for this paper.](#)

Displaying record number 471

| | | |
|-----------------------------|---|--------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | Pol(346-354) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Species (MHC/HLA)</u> | human(A*0201) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Experimental methods</u> | | |
| <u>Keywords</u> | epitope processing, immunodominance, escape | |

Notes

- Proteasome regulation influences epitope processing and could influence patterns of immunodominance.
- The proteasome is inhibited by lactacystin treatment, and gamma IFN induces expression of proteasome subunits, LMP2 and LMP7, which combine with the proteasome to create an immunoproteasome.
- IFN-gamma induction of the immunoproteasome and lactacystin inhibition increases the presentation of the A*0201 VIYQYMDDL epitope, but decreases the presentation of the A*0201 ILKEPVHGV epitope, which is immunodominant within pol proteins, showing the two epitopes are processed by different pathways.
- ILKEPVHGV seems to be processed by the classical proteasome pathway, while VIYQYMDDL appears to be destroyed by this pathway.
- This epitope contains the catalytic site (YMDD) of RT, a conserved sequence in HIV-1 which restricts escape mutants.

References

Sewell1999 A. K. Sewell, D. A. Price, H. Teisserenc, B. L. Booth, U. Gileadi, F. M. Flavin, J. Trowsdale, R. E. Phillips, and V. Cerundolo. IFN-gamma exposes a cryptic cytotoxic T lymphocyte epitope in HIV-1 reverse transcriptase. *J. Immunol.*, 162:7075-9, 1999. PubMed ID: 10358150. [Show all entries for this paper.](#)

Displaying record number 473

| | | |
|-----------------------------|-----------------|--------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | RT(346-354 LAI) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Subtype</u> | B | |
| <u>Species (MHC/HLA)</u> | human(A*0201) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Experimental methods</u> | | |
| <u>Keywords</u> | review | |

Notes

- The substitution VIYQYVDDL abrogates CTL response and confers drug resistance.
- Menendez-Arias1998, in a review, notes that this epitope includes catalytic residues (Asp-185 and Asp-186) in the active site of RT.

References

Harrer1996 E. Harrer, T. Harrer, P. Barbosa, M. Feinberg, R. P. Johnson, S. Buchbinder, and B. D. Walker. Recognition of the highly conserved YMDD region in the human immunodeficiency virus type 1 reverse transcriptase by HLA-A2-restricted cytotoxic T lymphocytes from an asymptomatic long-term nonprogressor. *J. Infect. Dis.*, 173:476-479, 1996. The amino acid stretch YMDD is a critical functional domain of reverse transcriptase, and is highly conserved. This sequence is also part of an HLA-A2-restricted epitope. The substitution YMDD to YVDD confers drug resistance to FTC and dideoxyinosine, and also abolishes the CTL specific response. PubMed ID: 8568316. Show all entries for this paper.

Menendez-Arias1998 L. Menendez-Arias, A. Mas, and E. Domingo. Cytotoxic T-lymphocyte responses to HIV-1 reverse transcriptase

(review). *Viral Immunol.*, 11:167-81, 1998. PubMed ID: [10189185](#). [Show all entries for this paper.](#)

Displaying record number 474

| | | |
|-----------------------------|-----------------|-----------------------------------|
| <u>HXB2 Location</u> | RT(179-187) | RT Epitope Map |
| <u>Author Location</u> | RT(346-354 LAI) | |
| <u>Epitope</u> | VIYQYMDDL | Epitope Alignment |
| <u>Subtype</u> | B | |
| <u>Species (MHC/HLA)</u> | human(A*0201) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Experimental methods</u> | | |
| <u>Keywords</u> | optimal epitope | |

Notes

- C. Brander notes this is an A*0201 epitope.

References

Frahm2008 Nicole Frahm, Brett Baker, and Christian Brander. Identification and Optimal Definition of HIV-Derived Cytotoxic T Lymphocyte (CTL) Epitopes for the Study of CTL Escape, Functional Avidity and Viral Evolution. In Bette Korber, Christian Brander, Barton F. Haynes, Richard Koup, John P. Moore, Bruce D. Walker, and David I. Watkins, editors, *HIV Molecular Immunology 2008*. page 3 ff. Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, 2008. URL: <http://www.hiv.lanl.gov/content/immunology>. [Show all entries for this paper.](#)

Displaying record number 477

| | | |
|----------------------|-------------|--------------------------------|
| <u>HXB2 Location</u> | RT(179-187) | RT Epitope Map |
|----------------------|-------------|--------------------------------|

Author Location RT(346-354)
Epitope VIYQYMDDL Epitope Alignment
Species (MHC/HLA) human(A*0201)
Immunogen HIV-1 infection
Experimental methods
Keywords review, escape

Notes

- Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope or evidence of immune escape.
- Only one subject had CTL against all three epitopes.
- Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area.
- In the review Menendez-Arias1998 the authors note that substitution of three residues in this epitope can confer resistance to RT inhibitors (1, 3, and 6) -- substitutions V1E and M6V abolish CTL activity, and M6V confers resistance to 3TC - - substitution Y3C reduces CTL activity and is associated with resistance to non-nucleoside RT inhibitors.

References

Brander1998 Christian Brander, Kelly E. Hartman, Alicja K. Trocha, Norman G. Jones, R. Paul Johnson, Bette Korber, Peggy Wentworth, Susan P. Buchbinder, Steve Wolinsky, Bruce D. Walker, and Spyros A. Kalams. Lack of Strong Immune Selection Pressure by the Immunodominant, HLA-A*0201-Restricted Cytotoxic T Lymphocyte Response in Chronic Human Immunodeficiency Virus-1 Infection. *J. Clin. Invest.*, 101(11):2559-2566, 1 Jun 1998. PubMed ID: 9616227. Show all entries for this paper.

Menendez-Arias1998 L. Menendez-Arias, A. Mas, and E. Domingo. Cytotoxic T-lymphocyte responses to HIV-1 reverse transcriptase

(review). *Viral Immunol.*, 11:167-81, 1998. PubMed ID: [10189185](#). [Show all entries for this paper.](#)

Displaying record number 1315

| | | | |
|-----------------------------|----------------------------------|------------------|----------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT</u> | <u>Epitope</u> |
| | | <u>Map</u> | |
| <u>Author Location</u> | RT | | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope</u> | |
| | | <u>Alignment</u> | |
| <u>Epitope Name</u> | RT VL9 | | |
| <u>Species</u> | human(A*0201) | | |
| <u>(MHC/HLA)</u> | | | |
| <u>Immunogen</u> | HIV-1 infection | | |
| <u>Experimental methods</u> | | | |
| <u>Keywords</u> | subtype | comparisons, | supertype, |
| | computational epitope prediction | | |

Notes

- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences -- 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 - - 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, including RT VL9, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2)
- RT VL9 was not recognized by any of the 22 HLA-A2 patients with chronic HIV-1 infection or the 13 HLA-A2 patients with acute HIV-1 infection included in this study.

References

Altfeld2001 M. A. Altfeld, B. Livingston, N. Reshamwala, P. T. Nguyen, M. M. Addo, A. Shea, M. Newman, J. Fikes, J. Sidney, P. Wentworth, R. Chesnut, R. L. Eldridge, E. S. Rosenberg, G. K. Robbins, C. Brander, P. E. Sax, S. Boswell, T. Flynn, S. Buchbinder, P. J. Goulder, B. D. Walker, A. Sette, and S. A. Kalams. Identification of novel HLA-A2-restricted human immunodeficiency virus type 1-specific cytotoxic T-lymphocyte epitopes predicted by the HLA-A2 supertype peptide-binding motif. *J. Virol.*, 75(3):1301-11, Feb 2001. URL: <http://jvi.asm.org/cgi/content/full/75/3/1301>. PubMed ID: 11152503. [Show all entries for this paper.](#)

Displaying record number 1355

| | | |
|-----------------------------|-----------------|--------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | RT(346-354) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Epitope Name</u> | VL9 | |
| <u>Species (MHC/HLA)</u> | human(A*0201) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Experimental methods</u> | | |
| <u>Keywords</u> | | |

Notes

- Integration of HIV RT CTL epitopes into the N-terminus of the HLA-A2 heavy chain, or tethering the epitopes to the target chain, resulted in epitope-specific lysis by CD8+ CTL.
- These antigens could also be used to stimulate primary responses *in vitro*.

References

DelaCruz2000 C. S. Dela Cruz, R. Tan, S. L. Rowland-Jones, and B. H. Barber. Creating HIV-1 reverse transcriptase cytotoxic T lymphocyte

target structures by HLA-A2 heavy chain modifications. *Int. Immunol.*,
12(9):1293-302, Sep 2000. URL:
<http://intimm.oupjournals.org/cgi/content/full/12/9/1293>. PubMed ID:
10967024. Show all entries for this paper.

Displaying record number 52264

| | | |
|---------------------------------------|--|------------------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | Pol(346-354) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope</u> <u>Alignment</u> |
| <u>Subtype</u> | B | |
| <u>Species (MHC/HLA)</u> | human(A*0201) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Experimental</u> <u>methods</u> | | |
| <u>Keywords</u> | epitope processing, immunodominance | |

Notes

- Epitope processing of three different HLA-A*0201 HIV epitopes was shown to use different pathways, which might influence patterns of immunodominance. .174 cells were used that lack TAP1 and TAP2 genes, as well as the LMP2 and LMP7 genes that encode the beta-subunits of the immunoproteasome. These genes could be added back through transfection to study processing.
- ILKEPVHGV was efficiently presented in TAP-1 and -2 transfected cells while VIYQYMDDL and SLYNTVATL were not. VIYQYMDDL was destroyed by the MB1 subunit of the protease, and could be expressed in the presence of the proteasome inhibitor lactacystin, but SLYNTVATL expression was not restored. SLYNTVATL expression was unaltered by lactacystin in a wild type cell line.

References

Sewell12002 Andrew K. Sewell, Bruce L. Booth, Jr., Vincenzo Cerundolo, Rodney E. Phillips, and David A. Price. Differential Processing of HLA A2-Restricted HIV Type 1 Cytotoxic T Lymphocyte Epitopes. *Viral Immunol.*, 15(1):193-196, 2002. PubMed ID: [11952141](#). [Show all entries for this paper.](#)

Displaying record number 52296

| | | | |
|-----------------------------|--------------------------|------------------|------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT</u> | <u>Epitope</u> |
| | | <u>Map</u> | |
| <u>Author Location</u> | RT(346-354 LAI) | | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope</u> | |
| | | <u>Alignment</u> | |
| <u>Epitope Name</u> | LR26 | | |
| <u>Subtype</u> | B | | |
| <u>Species</u> | | | |
| <u>(MHC/HLA)</u> | mouse (A*0201) | | |
| <u>Immunogen</u> | vaccine | | |
| <u>Experimental methods</u> | | | |
| <u>Keywords</u> | binding | affinity, | vaccine-specific |
| | epitope characteristics, | immunodominance | |

Vaccine Details

| | |
|-----------------------|---|
| <u>Vaccine type</u> | peptide |
| <u>Vaccine strain</u> | B clade LAI |
| <u>Adjuvant</u> | Incomplete Freund's Adjuvant (IFA), Montanide (ISA 720), P30, PLG |

Notes

- The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study -- ILKEPVHGV

(RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01).

- The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour.
- HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants.
- All peptides except VIYQYMDDL induced a strong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.

References

Peter2001 Katrin Peter, Ying Men, Giuseppe Pantaleo, Bruno Gander, and Giampietro Corradin. Induction of a Cytotoxic T-Cell Response to HIV-1 Proteins with Short Synthetic Peptides and Human Compatible Adjuvants. *Vaccine*, 19(30):4121-4129, 20 Jul 2001. PubMed ID: [11457536](#). [Show all entries for this paper.](#)

Displaying record number 52297

| | | | |
|------------------------|-----------------|------------------|----------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT</u> | <u>Epitope</u> |
| | | <u>Map</u> | |
| <u>Author Location</u> | RT(346-354 LAI) | | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope</u> | |
| | | <u>Alignment</u> | |
| <u>Epitope Name</u> | LR26 | | |
| <u>Subtype</u> | B | | |
| <u>Species</u> | | | |
| <u>(MHC/HLA)</u> | mouse(A*0201) | | |
| <u>Immunogen</u> | vaccine | | |

Experimental

methods

Keywords vaccine-specific epitope
characteristics, immunodominance

Vaccine Details

Vaccine type peptide

Vaccine strain B clade LAI

Adjuvant Incomplete Freund's Adjuvant (IFA), IL-12, P30

Notes

- When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination Peter2001. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macrophages in the spleen.

References

Peter2002 Katrin Peter, Michael J. Brunda, and Giampietro Corradin. IL-12 Administration Leads to a Transient Depletion of T Cells, B Cells, and APCs and Concomitant Abrogation of the HLA-A2.1-Restricted CTL Response in Transgenic Mice. *J. Immunol.*, 169(1):63-67, 1 Jul 2002. PubMed ID: 12077229. Show all entries for this paper.

Displaying record number 52442

EXB2 Location RT(179-187)

RT Epitope
Map

| | | |
|---------------------------------------|--|------------------------------------|
| <u>Author</u> | Pol | |
| <u>Location</u> | | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope</u> <u>Alignment</u> |
| <u>Subtype</u> | A, B, C, D | |
| <u>Species</u> <u>(MHC/HLA)</u> | human, macaque(A*0201) | |
| <u>Immunogen</u> | HIV-1 infection, vaccine | |
| <u>Experimental</u> <u>methods</u> | | |
| <u>Keywords</u> | subtype comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance | |

Vaccine Details

| | |
|--------------------------|---|
| <u>Vaccine type</u> | DNA prime with modified vaccinia Ankara (MVA) boost |
| <u>Vaccine strain</u> | A clade |
| <u>Vaccine component</u> | p17 Gag, p24 Gag |

Notes

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke2000.
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM),

included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002](#).

References

Hanke2000 Tomas Hanke and Andrew J. McMichael. Design and construction of an experimental HIV-1 vaccine for a year-2000 clinical trial in Kenya. *Nat. Med.*, 6(9):951-955, Sep 2000. PubMed ID: [10973301](#). [Show all entries for this paper.](#)

Wee2002 Edmund G.-T. Wee, Sandip Patel, Andrew J. McMichael, and Tom\ 'a\ v s Hanke. A DNA/MVA-Based Candidate Human Immunodeficiency Virus Vaccine for Kenya Induces Multi-Specific T Cell Responses in Rhesus Macaques. *J. Gen. Virol.*, 83(Pt 1):75-80, Jan 2002. PubMed ID: [11752703](#). [Show all entries for this paper.](#)

Displaying record number 52766

| | | |
|-----------------------------|---|--------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | RT(179-187) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Subtype</u> | B | |
| <u>Species (MHC/HLA)</u> | mouse(A*0201) | |
| <u>Immunogen</u> | vaccine | |
| <u>Donor MHC/HLA</u> | A2.1 | |
| <u>Experimental methods</u> | Chromium-release assay, Cytokine production | |
| <u>Keywords</u> | binding affinity, vaccine-induced epitopes | |

Vaccine Details

Vaccine type peptide

Vaccine component RT

Adjuvant Incomplete Freund's Adjuvant (IFA), IL-12

Notes

- Alanine substitutions of VIYQYMDDL were tested for importance of each amino acid for HLA-A2.1 binding. Peptide variant (vLyqymddV) showed an 8 fold higher MHC binding affinity than wild type. YLyqymddV had an even higher binding affinity, but the Y at position one blocked TCR recognition. The higher affinity form of vLyqymddV induced CTL *in vivo* that could protect against a vaccinia virus expressing RT and the wild type epitope.

References

Okazaki2003 Takahiro Okazaki, C. David Pendleton, François Lemonnier, and Jay A. Berzofsky. Epitope-Enhanced Conserved HIV-1 Peptide Protects HLA-A2-Transgenic Mice Against Virus Expressing HIV-1 Antigen. *J. Immunol.*, 171(5):2548-2555, Sep 2003. PubMed ID: [12923405](#).
[Show all entries for this paper.](#)

Displaying record number 53004

| | | | |
|----------------------|-----------------------------------|------------------|----------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT</u> | <u>Epitope</u> |
| <u>Author</u> | | <u>Map</u> | |
| <u>Location</u> | RT(179-187 MN) | | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope</u> | |
| <u>Subtype</u> | B | <u>Alignment</u> | |
| <u>Species</u> | | | |
| <u>(MHC/HLA)</u> | humanized mouse(A*0201) | | |
| <u>Immunogen</u> | vaccine | | |
| <u>Experimental</u> | | | |
| <u>methods</u> | CD8 T-cell Elispot - IFN γ | | |

Keywords epitope processing, vaccine-specific
epitope characteristics, immunodominance,
immunotherapy

Vaccine Details

Vaccine type DNA, polyepitope

Vaccine strain B clade MN

Vaccine component gp120, Protease, RT

Adjuvant Incomplete Freund's Adjuvant (IFA)

Notes

- Immunization of HLA-A*0201-transgenic mice with synthetic genes encoding clusters of human A*0201 CTL epitopes located at the sites of drug resistance mutations, induced RT-specific cellular responses indicating the immunogenicity of these constructs. This vaccine strategy may be a first step towards a therapeutic vaccine against drug-resistant strains.
- This was one of five HLA-A*0201 epitopes from the RT or protease proteins that was included in the polyepitope vaccine. When the transgenic HLA A*0202 mice were vaccinated with the polyepitope construct or with a mixture of RT peptides, a sustained low level CD8+ T-cell gamma IFN response was observed, in contrast to when an intact RT gene was used for vaccination.

References

Isaguliant2004 Maria G. Isaguliant, Bartek Zuber, Andreas Boberg, Dan Sjöstrand, Sergey V. Belikov, Erik Rollman, Anne Kjerrström Zuber, Vladimir O. Rechinsky, Ann-Sofie Rytting, Clas F. R. Källander, Jorma Hinkula, Sergey N. Kochetkov, Margaret Liu, and Britta Wahren. Reverse Transcriptase-Based DNA Vaccines against Drug-Resistant HIV-1 Tested in a Mouse Model. *Vaccine*, 22(13-14):1810-1819, 16 Apr 2004. PubMed ID: [15068865](#). [Show all entries for this paper.](#)

Displaying record number 53026

| | | | |
|------------------------|--|------------------|----------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT</u> | <u>Epitope</u> |
| | | <u>Map</u> | |
| <u>Author Location</u> | Pol(346-354) | | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope</u> | |
| | | <u>Alignment</u> | |
| <u>Subtype</u> | B | | |
| <u>Species</u> | human(A*0201) | | |
| <u>(MHC/HLA)</u> | | | |
| <u>Immunogen</u> | HIV-1 infection | | |
| <u>Country</u> | United States | | |
| <u>Experimental</u> | CD8 T-cell Elispot - IFN γ , CD8 T-cell | | |
| <u>methods</u> | Elispot granzyme B | | |
| <u>Keywords</u> | Th1, characterizing CD8+ T cells | | |

Notes

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- One of seven patients responded to this peptide with GzB producing cells, while none of the patients responded with IFN-gamma producing cells.

References

Kleen2004 Thomas O. Kleen, Robert Asaad, Samuel J. Landry, Bernhard O. Boehm, and Magdalena Tary-Lehmann. Tc1 Effector Diversity Shows Dissociated Expression of Granzyme B and Interferon-gamma in HIV Infection. *AIDS*, 18(3):383-392, 20 Feb 2004. PubMed ID: [15090789](#). [Show all entries for this paper.](#)

Displaying record number 54001

| | | |
|-----------------------------|--------------------------------------|--------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>PT Epitope Map</u> |
| <u>Author Location</u> | (C consensus) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Subtype</u> | C | |
| <u>Species (MHC/HLA)</u> | human(A*0201) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Country</u> | South Africa | |
| <u>Experimental methods</u> | CD8 T-cell Elispot - IFN γ | |
| <u>Keywords</u> | rate of progression, optimal epitope | |

Notes

- A comprehensive analysis of 160 class I T cell responses in 578 individuals from KwaZulu-Natal, South Africa was performed. Gag-specific responses were associated with lowering viremia, while Env, accessory and regulatory protein-specific responses were associated with higher viremia.
- VIYQYMDDL is an optimal epitope.

References

Kiepiela2007 Photini Kiepiela, Kholiswa Ngumbela, Christina Thobakgale, Dhanwanthie Ramduth, Isobella Honeyborne, Eshia Moodley, Shabashini Reddy, Chantal de Pierres, Zenele Mncube, Nompumelelo Mkhwanazi, Karen Bishop, Mary van der Stok, Kriebashnie Nair, Nasreen Khan, Hayley Crawford, Rebecca Payne, Alasdair Leslie, Julia Prado, Andrew Prendergast, John Frater, Noel McCarthy, Christian Brander, Gerald H. Learn, David Nickle, Christine Rousseau, Hoosen Coovadia, James I. Mullins, David Heckerman, Bruce D. Walker, and Philip Goulder. CD8+ T-Cell Responses to Different HIV Proteins Have Discordant Associations with Viral Load. *Nat. Med.*, 13(1):46-53, Jan 2007. PubMed ID: [17173051](#). [Show all entries for this paper.](#)

Displaying record number 54314

| | | | |
|----------------------|--|------------------|----------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT</u> | <u>Epitope</u> |
| <u>Author</u> | | <u>Map</u> | |
| <u>Location</u> | RT(179-187) | | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope</u> | |
| <u>Species</u> | | <u>Alignment</u> | |
| <u>(MHC/HLA)</u> | human (A*0201) | | |
| <u>Immunogen</u> | HIV-1 infection | | |
| <u>Experimental</u> | CD8 T-cell Elispot - IFN γ , Chromium-release | | |
| <u>methods</u> | assay, Cytokine production, HLA binding, | | |
| | Other | | |
| <u>Keywords</u> | vaccine-specific epitope characteristics, | | |
| | cross-presentation by different HLA, HLA | | |
| | associated polymorphism | | |

Notes

- 25 CTL epitopes with sequence conservation were studied. Population protection coverage (PPC) for 5 different ethnic groups in the US was estimated by combining HLA binding predictions and known HLA frequencies. HIV-1-naive individuals mounted a better response to the epitope pools than HIV-1 infected individuals.
- A more detailed evaluation of HIV-naive T-cell responses was undertaken, limiting the study to only those peptides that are restricted to A*0201. Though the peptides could cross-recognize and bind different HLA, they were able to specifically lyse only cells of the same (A*0201) HLA-restriction. Thus, the CTL response was less degenerate than peptide binding to MHC.
- This epitope, VIYQYMDDL, was predicted to be restricted by HLA A*0201, A*0205, A*0207, A*0214.

References

Reche2006 Pedro A. Reche, Derin B. Keskin, Rebecca E. Hussey, Petronela Ancuta, Dana Gabuzda, and Ellis L. Reinherz. Elicitation from Virus-Naive Individuals of Cytotoxic T Lymphocytes Directed against Conserved HIV-1 Epitopes. *Med. Immunol.*, 5:1, 2006. PubMed ID: 16674822. [Show all entries for this paper.](#)

Displaying record number 55288

| | | | |
|----------------------|--|----------------|------------------|
| <u>HYB2 Location</u> | RT(179-187) | <u>RT</u> | <u>Epitope</u> |
| | | <u>Map</u> | |
| <u>Author</u> | Pol | | |
| <u>Location</u> | | | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope</u> | <u>Alignment</u> |
| <u>Subtype</u> | B | | |
| <u>Species</u> | human(A*0201, A*19, B*3501, B*44, Cw*07, | | |
| <u>(MHC/HLA)</u> | Cw*16) | | |
| <u>Immunogen</u> | HIV-1 infection | | |
| <u>Donor MHC/HLA</u> | A*01, A*19, B*14, B*44, Cw*08, Cw*16 | | |
| <u>Country</u> | United States | | |
| <u>Experimental</u> | CD8 T-cell Elispot - IFN γ , Other | | |
| <u>methods</u> | | | |
| <u>Keywords</u> | HAART, ART, mother-to-infant transmission, rate of progression, co-receptor, immune evasion, HLA associated polymorphism | | |

Notes

- HIV-1 mother-to-child transmission is studied for LTNP by comparing entire genomes from 2 mother (M1, M2) and 2 daughter (D1, D2) RNA samples of a mother-child pair over 11 years. Genetic distance was 94% between subjects' strains. Divergence in sequences was attributed to distinct HLA selection pressures as ds/dn was larger for intra- rather than inter-person sequences.

10 new mutations in D2 were found related to unique daughter HLA alleles.

- Functional ELISpot studies using D2 and Nef peptides reveal strong associations between CTL responses and escape variants, contributing to delayed progression.
- LTNP status was not related to defective virus since all viral genes were intact and CTL response did not effectively control viral load. It is supposed that genetic HLA background and HIV-1 epitope-immune response interaction account for nonprogression of disease.
- All isolates contained R77Q in Vpr, a variation associated with reduction of cellular apoptosis.
- This HLA-A*02/A*0201 restricted epitope, VIYQYMDDL was mutated to cIYQYMDDL in the daughter D2 isolate.

References

Reinis2007 Milan Reinis, Barbara Weiser, Carla Kuiken, Tao Dong, Dorothy Lang, Sharon Nachman, Yonghong Zhang, Sarah Rowland-Jones, and Harold Burger. Genomic Analysis of HIV Type 1 Strains Derived from a Mother and Child Pair of Long-Term Nonprogressors. *AIDS Res. Hum. Retroviruses*, 23(2):309-315, Feb 2007. PubMed ID: [17331038](#). [Show all entries for this paper.](#)

Displaying record number 469

| | | |
|-----------------------------|--------------|--------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | Pol(346-354) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Species (MHC/HLA)</u> | human(A2) | |
| <u>Immunogen</u> | vaccine | |
| <u>Experimental methods</u> | | |
| <u>Keywords</u> | | |

Vaccine Details

Vaccine type DNA prime with vaccinia boost

Notes

- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2.
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d -- this transgene is the only MHC molecule expressed in the mice.
- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost.
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFD SRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope -- one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested.
- VIYQYMDDL was recognized by 3 of the HLA-A2 patients.

References

Woodberry1999 T. Woodberry, J. Gardner, L. Mateo, D. Eisen, J. Medveczky, I. A. Ramshaw, S. A. Thomson, R. A. Ffrench, S. L. Elliott, H. Firat, F. A. Lemonnier, and A. Suhrbier. Immunogenicity of a human immunodeficiency virus (HIV) polytope vaccine. *J. Virol.*, 73:5320-5, 1999. PubMed ID: [10364276](#). [Show all entries for this paper.](#)

Displaying record number 472

HXB2 Location

RT(179-187)

RT Epitope Map

| | | |
|-----------------------------|-----------------------|--------------------------|
| <u>Author Location</u> | RT(179-187) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Species (MHC/HLA)</u> | human(A2) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Experimental methods</u> | | |
| <u>Keywords</u> | escape, immunotherapy | |

Notes

- The mutation M184V confers resistance to lamivudine, and is in the middle of the HLA-A2 epitope VIYQYMDDL.
- 1/28 individuals tested produced HIV-1 RT-specific CTL that recognized the peptide representing the lamivudine escape mutants VIYQYVDDL and VIYQYIDDL, but failed to recognize the wildtype epitope VIYQYMDDL.
- This suggests immunotherapy stimulating anti-VIYQYVDDL responses maybe helpful for reducing lamivudine escape.

References

Schmitt2000 M. Schmitt, E. Harrer, A. Goldwich, M. Bauerle, I. Graedner, J. R. Kalden, and T. Harrer. Specific recognition of lamivudine-resistant HIV-1 by cytotoxic T lymphocytes. *AIDS*, 14:653-8, 2000. PubMed ID: [10807188](#). [Show all entries for this paper.](#)

Displaying record number 475

| | | |
|-----------------------------|-----------------|--------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | RT(179-187) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Species (MHC/HLA)</u> | human(A2) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Experimental methods</u> | | |
| <u>Keywords</u> | | |

Notes

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol -- RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)

References

Haas1998 G. Haas, A. Samri, E. Gomard, A. Hosmalin, J. Duntze, J. M. Bouley, H. G. Ihlenfeldt, C. Katlama, and B. Autran. Cytotoxic T cell responses to HIV-1 reverse transcriptase, integrase and protease. *AIDS*, 12(12):1427-36, 1998. PubMed ID: [9727563](#). [Show all entries for this paper.](#)

Displaying record number 1731

| | | |
|-----------------------------|--|--------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | Pol(339-347 93TH253 subtype CRF01) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Epitope Name</u> | P334-342 | |
| <u>Subtype</u> | CRF01_AE | |
| <u>Species (MHC/HLA)</u> | human (A2) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Experimental methods</u> | | |
| <u>Keywords</u> | HIV exposed persistently seronegative (HEPS) | |

Notes

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers -- weak CTL responses were detected in 4/7

HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.

- This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2.

References

Sriwanthana2001 B. Sriwanthana, T. Hodge, T. D. Mastro, C. S. Dezzutti, K. Bond, H. A. Stephens, L. G. Kostrikis, K. Limpakarnjanarat, N. L. Young, S. H. Qari, R. B. Lal, D. Chandanayingyong, and J. M. McNicholl. HIV-specific cytotoxic T lymphocytes, HLA-A11, and chemokine-related factors may act synergistically to determine HIV resistance in CCR5 delta32-negative female sex workers in Chiang Rai, northern Thailand. *AIDS Res. Hum. Retroviruses*, 17(8):719-34, 20 May 2001. PubMed ID: [11429112](#). [Show all entries for this paper.](#)

Displaying record number 1748

| | | |
|---------------------------------|---|------------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | Pol(339-347 93TH253 subtype CRF01) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Subtype</u> | CRF01_AE | |
| <u>Species (MHC/HLA)</u> | human(A2) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Experimental methods</u> | | |
| <u>Keywords</u> | subtype comparisons | |

Notes

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade

versions of previously defined B-clade A2 and A24 epitopes were also tested.

- 2/4 tested FSWs recognized the E clade version of this epitope, which is identical to the previously defined B clade version VIYQYMDDL.
- This epitope was conserved in many subtypes, and exact matches were very uncommon.

References

Bond2001 K. B. Bond, B. Sriwanthana, T. W. Hodge, A. S. De Groot, T. D. Mastro, N. L. Young, N. Promadej, J. D. Altman, K. Limpakarnjanarat, and J. M. McNicholl. An HLA-directed molecular and bioinformatics approach identifies new HLA-A11 HIV-1 subtype E cytotoxic T lymphocyte epitopes in HIV-1-infected Thais. *AIDS Res. Hum. Retroviruses*, 17(8):703-17, 20 May 2001. PubMed ID: [11429111](#).
[Show all entries for this paper.](#)

Displaying record number 1767

| | | |
|-----------------------------|--|--------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | RT(179-187) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Species (MHC/HLA)</u> | human (A2) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Experimental methods</u> | | |
| <u>Keywords</u> | rate of progression, acute/early infection | |

Notes

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two

with acute infection, five with chronic, and one long-term non-progressor (LTNP)

- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.

References

Day2001 C. L. Day, A. K. Shea, M. A. Altfeld, D. P. Olson, S. P. Buchbinder, F. M. Hecht, E. S. Rosenberg, B. D. Walker, and S. A. Kalams. Relative dominance of epitope-specific cytotoxic T-lymphocyte responses in human immunodeficiency virus type 1-infected persons with shared HLA alleles. *J. Virol.*, 75(14):6279-91, Jul 2001. URL: <http://jvi.asm.org/cgi/content/full/75/14/6279>. PubMed ID: [11413294](#).
[Show all entries for this paper.](#)

Displaying record number 52178

| | | |
|-----------------------------|--------------------------------|--------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | Pol(346-354 LAI) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Subtype</u> | B | |
| <u>Species (MHC/HLA)</u> | human(A2) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Experimental methods</u> | | |
| <u>Keywords</u> | HAART, ART, epitope processing | |

Notes

- Ritonavir (RTV) inhibits chymotryptic activity in the 20S proteasome *in vitro*, as does Saquinavir (SQV) to a lesser extent; Indinavir (IDV) does not. Thus there is concern protease inhibitors may adversely effect CTL epitope processing, but this paper indicates that processing is not inhibited at

therapeutically relevant concentrations of RTV when the proteasome is functioning in an intracellular context.

- RTV did not alter the presentation two RT A2 epitopes processed by distinct pathways: ILKEPVHGV, generated by the constitutive proteasome containing the MB1 beta subunit, and VIYQYMDDL which is dependent on IFNgamma induction of LMP7 which replaces MB1 in the immunoproteasome, and is destroyed by MB1 in the constitutive proteasome.
- RTV did not inhibit the processing and assembly of HLA-B35 or -A2, which are assembled with a rapid and moderate time course, respectively, or of HLA-A3, -B27 and -B39.

References

Kelleher2001a A. D. Kelleher, B. L. Booth, Jr., A. K. Sewell, A. Oxenius, V. Cerundolo, A. J. McMichael, R. E. Phillips, and D. A. Price. Effects of Retroviral Protease Inhibitors on Proteasome Function and Processing of HIV-Derived MHC Class I-Restricted Cytotoxic T Lymphocyte Epitopes. *AIDS Res. Hum. Retroviruses*, 17(11):1063-1066, 20 Jul 2001. PubMed ID: [11485623](#). [Show all entries for this paper.](#)

Displaying record number 52698

| | | |
|---------------------------------------|--|------------------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope</u> <u>Map</u> |
| <u>Author Location</u> | Pol(334-) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope</u> <u>Alignment</u> |
| <u>Epitope Name</u> | Pol334 | |
| <u>Species</u> <u>(MHC/HLA)</u> | human(A2) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Experimental</u> <u>methods</u> | CD8 T-cell Elispot - IFN γ , Chromium- release assay, Flow cytometric T-cell | |

cytokine assay

Keywords

binding affinity, subtype comparisons,
computational epitope prediction

Notes

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This epitope was one of the previously identified HLA-A2 epitopes studied.
- 1/17 HIV-infected HLA-A2+ people in this study recognized this epitope.

References

Corbet2003 Sylvie Corbet, Henrik Vedel Nielsen, Lasse Vinner, Sanne Lauemoller, Dominic Therrien, Sheila Tang, Gitte Kronborg, Lars Mathiesen, Paul Chaplin, Søren Brunak, Søren Buus, and Anders Fomsgaard. Optimization and Immune Recognition of Multiple Novel Conserved HLA-A2, Human Immunodeficiency Virus Type 1-Specific CTL Epitopes. *J. Gen. Virol.*, 84(Pt 9):2409-2421, Sep 2003. PubMed ID: [12917462](#). [Show all entries for this paper.](#)

Displaying record number 52967

| | | | |
|------------------------|--------------|------------------|----------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT</u> | <u>Epitope</u> |
| | | <u>Map</u> | |
| <u>Author Location</u> | Pol(334-342) | | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope</u> | |
| | | <u>Alignment</u> | |
| <u>Species</u> | | | |
| <u>(MHC/HLA)</u> | human (A2) | | |

| | |
|-----------------------------|--|
| <u>Immunogen</u> | HIV-1 infection |
| <u>Donor MHC/HLA</u> | A02, B35, Bw62 |
| <u>Experimental methods</u> | Chromium-release assay, Flow cytometric T-cell cytokine assay, proliferation |
| <u>Keywords</u> | HAART, ART, memory cells, immune dysfunction |

Notes

- HAART restores HIV specific immunity after advanced infection by increase of CD4+ and CD8+ T cell numbers after supression of viral replication. However, HIV specific CTLs emerged only with detectable viral replication breakthroughs and were short-lived while CD4+ T-cell responses remained compromised, suggesting failure of generating stable CD8+ memory T-cells in the absence of HIV-specific T-helper responses.

References

Gamberg2004 Jane Gamberg, Lisa Barrett, Ian Bowmer, Constance Howley, and Michael Grant. Immune Reconstitution and Viral Stimulation Are Required to Restore HIV-Specific CD8 T Cell Responses Following Advanced Infection. *J. Clin. Immunol.*, 24(2):115-124, Mar 2004. PubMed ID: [15024178](#). [Show all entries for this paper.](#)

Displaying record number 53054

| | | | |
|------------------------|-------------|------------------|----------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT</u> | <u>Epitope</u> |
| <u>Author Location</u> | RT(179-187) | <u>Map</u> | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope</u> | |
| <u>Subtype</u> | B | <u>Alignment</u> | |
| <u>Species</u> | human (A2) | | |
| <u>(MHC/HLA)</u> | | | |

| | |
|-----------------------------|--|
| <u>Immunogen</u> | HIV-1 infection |
| <u>Country</u> | Canada |
| <u>Experimental methods</u> | CD8 T-cell Elispot - IFN γ , Chromium-release assay |
| <u>Keywords</u> | HAART, ART, immunotherapy, variant cross-recognition or cross-neutralization |

Notes

- Accumulation of specific antiretroviral drug-resistance mutations in Pol gene was shown to sustain and even enhance the antigenicity and immunogenicity of HIV-1 CTL epitopes in this region. Several different patterns of cross-reactivity and selective recognition of wild-type and variant epitopes were found.
- VICQYMDDL, VIYQYvDDL and VICQYvDDL variants are detected due to appearance of Y181C and M184V resistance mutations. The double mutant was the only form recognized in one A02 treated individual, the epitope was not recognized in another.

References

Mason2004 Rosemarie D. Mason, M. Ian Bowmer, Constance M. Howley, Maureen Gallant, Jennifer C. E. Myers, and Michael D. Grant. Antiretroviral Drug Resistance Mutations Sustain or Enhance CTL Recognition of Common HIV-1 Pol Epitopes. *J. Immunol.*, 172(11):7212-7219, 1 Jun 2004. PubMed ID: [15153547](#). [Show all entries for this paper.](#)

Displaying record number 53574

| | | | |
|------------------------|-------------|------------------|----------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT</u> | <u>Epitope</u> |
| <u>Author Location</u> | RT(179-187) | <u>Map</u> | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope</u> | |
| | | <u>Alignment</u> | |

| | |
|-----------------------------|---|
| <u>Subtype</u> | B |
| <u>Species</u> (MHC/HLA) | human (A2) |
| <u>Immunogen</u> | HIV-1 infection |
| <u>Country</u> | United States |
| <u>Experimental methods</u> | CD8 T-cell Elispot - IFN γ , Chromium-release assay, HLA binding |
| <u>Keywords</u> | acute/early infection, optimal epitope |

Notes

- The most frequently targeted HLA-A2-restricted CD8+ T-cell epitopes in chronic infection were significantly less frequently recognized during primary infection. This epitope was only recognized in chronic infection.

References

Altfeld2005a Marcus Altfeld, Todd M. Allen, Elizabeth T. Kalife, Nicole Frahm, Marylyn M. Addo, Bianca R. Mothe, Almas Rathod, Laura L. Reyor, Jason Harlow, Xu G. Yu, Beth Perkins, Loren K. Robinson, John Sidney, Galit Alter, Mathias Lichterfeld, Alessandro Sette, Eric S. Rosenberg, Philip J. R. Goulder, Christian Brander, and Bruce D. Walker. The Majority of Currently Circulating Human Immunodeficiency Virus Type 1 Clade B Viruses Fail To Prime Cytotoxic T-Lymphocyte Responses against an Otherwise Immunodominant HLA-A2-Restricted Epitope: Implications for Vaccine Design. *J. Virol.*, 79(8):5000-5005, Apr 2005. PubMed ID: [15795285](#). [Show all entries for this paper.](#)

Displaying record number 53624

| | |
|------------------------|------------------|
| <u>HXB2 Location</u> | RT(179-187) |
| <u>Author Location</u> | RT(179-187 HXB2) |
| <u>Epitope</u> | VIYQYMDDL |

| | |
|------------|------------------|
| <u>RT</u> | <u>Epitope</u> |
| <u>Map</u> | |
| | <u>Epitope</u> |
| | <u>Alignment</u> |

| | |
|---------------------------------------|---|
| <u>Epitope Name</u> | 51F |
| <u>Subtype</u> | B |
| <u>Species</u> <u>(MHC/HLA)</u> | transgenic mouse(A2) |
| <u>Immunogen</u> | vaccine |
| <u>Experimental</u> <u>methods</u> | CD8 T-cell Elispot - IFN γ , Chromium-release assay, Cytokine production |
| <u>Keywords</u> | vaccine-specific epitope characteristics, vaccine antigen design |

Vaccine Details

| | |
|--------------------------|----------------------------|
| <u>Vaccine type</u> | DNA |
| <u>Vaccine strain</u> | multiple epitope immunogen |
| <u>Vaccine component</u> | p17/p24 Gag, Pol |
| <u>Adjuvant</u> | IL-12 |

Notes

- Immunization of transgenic mice with a codon-optimized hGagp17p24-Polp51 DNA plasmid, consisting of clusters of highly conserved CTL epitopes presented by multiple MHC class I alleles, induced 2- to 5-fold higher CD8+ T-cell responses than the corresponding full-length proteins. The modified proteins had the ribosomal frameshift deleted, as well as the potentially immunosuppressive p15, and protease and integrase. This correlated with higher protection against challenge with Gag and Pol expressing recombinant vaccinia virus. Mice immunized with the hGagp17p24-Polp51 also showed an elevated level of type 1 cytokine production as well as an increased titer of p24- and RT-specific IgG2 antibody responses.
- This was 1 of 4 A2 gag/pol epitopes tested. Transgenic mice immunized with the deleted construct induced more potent EliSpot reactions to this epitope than those immunized with full length Gag/Pol.

References

Bolesta2005a Elizabeth Bolesta, Jaroslaw Gzyl, Andrzej Wierzbicki, Dariusz Kmiecniak, Aleksandra Kowalczyk, Yutaro Kaneko, Alagarsamy Srinivasan, and Danuta Kozbor. Clustered Epitopes within the Gag-Pol Fusion Protein DNA Vaccine Enhance Immune Responses and Protection against Challenge with Recombinant Vaccinia Viruses Expressing HIV-1 Gag and Pol Antigens. *Virology*, 332(2):467-479, 20 Feb 2005. PubMed ID: [15680412](#). [Show all entries for this paper.](#)

Displaying record number 53860

| | | |
|-----------------------------|--|--------------------------|
| <u>HXB2 Location</u> | RT(179-187) | <u>RT Epitope Map</u> |
| <u>Author Location</u> | RT(346-354) | |
| <u>Epitope</u> | VIYQYMDDL | <u>Epitope Alignment</u> |
| <u>Epitope Name</u> | VL9 | |
| <u>Species (MHC/HLA)</u> | human(A2) | |
| <u>Immunogen</u> | HIV-1 infection | |
| <u>Country</u> | Germany | |
| <u>Experimental methods</u> | CD8 T-cell Elispot - IFN γ , Chromium-release assay | |
| <u>Keywords</u> | HAART, ART, optimal epitope | |

Notes

- CTL responses to 3 HLA-A2-restricted epitopes were investigated in 51 HIV-1 infected HLA-A2+ individuals. The most prevalent response was seen for IV9, followed by SL9. The VL9 epitope was not recognized.

References

Schmitt-Haendle2005 Matthias Schmitt-Haendle, Oliver Bachmann, Ellen Harrer, Barbara Schmidt, Michael Bäuerle, and Thomas Harrer. Recognition Patterns of HLA-A2-Restricted Human Immunodeficiency Virus-1-Specific Cytotoxic T-Lymphocytes in a Cohort of HIV-1-Infected

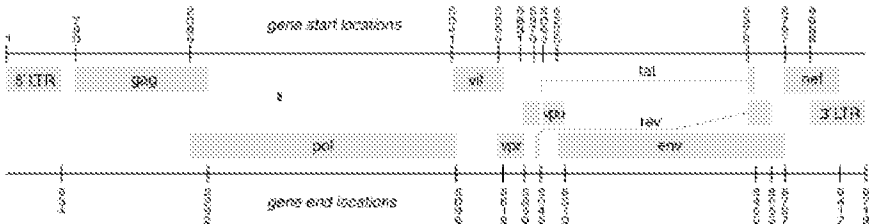
Individuals. *Viral Immunol.*, 18(4):627-636, 2005. PubMed ID: [16359229](#).
[Show all entries for this paper.](#)

Questions or comments? Contact us at immuno@lanl.gov

QuickAlign Results

Explanation of the results

Query location shown as colored bar in map between reading frames 1 and 2.



| | |
|-----------------|--|
| Query: seq1 | VIYQYMDDL |
| Query Length: | 9 |
| HXB2 Location: | genome: 3084→3110, region: Pol 333→341 |
| alignment used: | HIV1 Pol Protein, 1171 sequences |

Summarize All

Summarize By Subtype

Find Other Matches

"-" = identity to query sequence
 "." = gap in sequence
 "RED" = perfect identity to query sequence

| | | | |
|----------------------------------|--------|-----------|---|
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 N.CM.04.04CM_1131_03.DQ017383 I-----
 N.CM.95.YBF30.AJ006022 I-----
 N.CM.97.YBF106.AJ271370 I-----
 O.BE.87.ANT70.L20587 E-C-----
 O.CM.91.MVP5180.L20571 E----I---
 O.CM.96.96CMA102.AY169803 E-C-----
 O.CM.96.96CMABB009.AY169806 E-C-----
 O.CM.96.96CMABB637.AY169810 E-----
 O.CM.97.97CMABB447.AY169813 E-C-----
 O.CM.97.97CMABB497.AY169809 E-----
 O.CM.98.98CMA104.AY169802 E-C-----
 O.CM.98.98CMA105.AY169816 E-C-----
 O.CM.98.98CMABB141.AY169807 E-C-----
 O.CM.98.98CMABB197.AY169811 E-C-----
 O.CM.98.98CMABB212.AY169804 E-C-----

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  O.CM.x.pCMO2_3.AY618998 E-C-----
    O.FR.92.VAU.AF407418 E-----
      O.SN.99.SEMP1300.AJ302647 E-C-----
O.US.97.97US08692A.AY169805 Q-C-----
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  CPZ.CM.05.SIVcpzLB7.DQ373064 -----
    CPZ.CM.05.SIVcpzMB66.DQ373063 I-----
CPZ.CM.05.SIVcpzMT145.DQ373066 I-----
  CPZ.CM.98.CAM3.AF115393 I-----
    CPZ.CM.98.CAM5.AJ271369 I-----
      CPZ.GA.88.GAB1.X52154 T-----

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Matching done using program ALIGN0, Myers and Miller, *CABIOS* 4:11-17 (1991)

Questions or comments? Contact us at seq-info@lanl.gov.